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PII: S2590-1095(21)00093-8
DOI: https://doi.org/10.1016/j.arrct.2021.100177
Reference: ARRCT 100177

To appear in: *Archives of Rehabilitation Research and Clinical Translation*

Please cite this article as: Margareta Gonzalez Lindh , Gustav Mattsson , Hirsh Koyi , Monica Blom Johansson , Robin Razmi , Andreas Palm , Swallowing function in COVID-19 patients after invasive mechanical ventilation, *Archives of Rehabilitation Research and Clinical Translation* (2021), doi: https://doi.org/10.1016/j.arrct.2021.100177

Swallowing function in COVID-19 patients after invasive mechanical ventilation

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Running head: Swallowing function in COVID-19 patients

Word count: 2723

Acknowledgements: This study was funded by the Centre for Research and Development Uppsala University/County Council of Gävleborg. We thank Christian Ehrenborg, MD PhD,

Department of infectious diseases in Region Gävleborg, the Speech Pathology Department in Gävleborg and research assistant Ingrid Olson.

Keywords: COVID-19, dysphagia, intensive care, invasive mechanical ventilation, swallowing

Competing interests: GM has received fees from Alnylam, Internetmedicin, and Merck, Sharp and Dohme. MGL, HK, MBJ, RR and AP declare no competing interests.

Abstract

Objective: To explore swallowing function and risk factors associated with delayed recovery of swallowing in COVID-19 patients post invasive mechanical ventilation using the Functional Oral Intake Scale (FOIS).

Design: Longitudinal cohort study.

Setting: 3 secondary-level hospitals.

Participants: Invasively ventilated patients (n=28), hospitalized with severe COVID-19 who were referred to the Speech and Language Pathology (SLP) departments post mechanical ventilation between March 5 and July 5 2020 for an evaluation of swallowing function before commencing oral diet.

Interventions: SLP assessment, advice and therapy for dysphagia.

Main outcome measures: Oral intake levels at baseline and hospital discharge according to the Functional Oral Intake Scale (FOIS). Patients were stratified according to FOIS (1-5=dysphagia, 6-7= functional oral intake). Data regarding comorbidities, frailty, intubation and tracheostomy, proning and SLP evaluation were collected.

Results

Dysphagia was found in 71% of the patients at baseline (in total 79% male, age 61 ±12 years, BMI 30 ±8 kg/m^2). Median FOIS score at baseline was 2 (IQR 1) vs 5 (IQR 2.5) at hospital discharge. Patients with dysphagia were older (64 ±8.5 vs 53 ±16 years; p= 0.019), had a higher incidence of hypertension (70% vs 12%; p=0.006) were ventilated invasively longer (16 ±7 vs 10 ±2 days; p=0.017) or with tracheostomy (9 ±9 vs 1 ±2 days; p=0.03) longer. A negative association was found between swallowing dysfunction at bedside and days hospitalized (r=-0.471, p=0.01), and number of days at the Intensive Care Unit (ICU) (r=-0.48, p=0.01).

Conclusion

Dysphagia is prevalent in COVID-19 patients post invasive mechanical ventilation and is associated with number of days in hospital and number of days in the ICU. Swallowing function and tolerance of oral diet improved at discharge (p<0.001).

Keywords: COVID-19, dysphagia, intensive care, invasive mechanical ventilation, swallowing function, frailty.

List of abbreviations: COVID-19, corona virus disease 2019; FOIS, Functional Oral Intake Scale; SLP, Speech and Language Pathology, ICU, Intensive Care Unit, IQR, Inter Quartile Ratio; BMI, Body Mass Index.

Introduction

During the first surge of the corona virus disease 2019 (COVID-19) pandemic, between 7-8% of patients hospitalized with Covid-19 were admitted to the Intensive Care Unit (ICU)[1]. The primary reason was respiratory failure. Dysphagia (swallowing dysfunction) is prevalent post

prolonged mechanical ventilation (>48 hours) [2]. Invasive ventilation can have a negative effect on laryngeal competence and swallowing physiology [2, 3] due to oedema, vocal fold immobility, reduced sensation and muscle disuse [4]. Time intubated is the strongest risk factor for dysphagia following invasive mechanical ventilation, incidence varying depending on which cohort is studied and how dysphagia is defined.

A systematic review by Skoretz, Flowers and Martino [5] of 14 studies on a total of 3520 patients (medical, surgical and cardiovascular surgical) following endotracheal intubation found a reported dysphagia frequency ranging from 3% to 62% where the highest dysphagia frequencies included patients experiencing prolonged intubation (>24 hours). More than half of the included studies reported a dysphagia frequency exceeding 20% and dysphagia was associated with pneumonia, prolonged treatment of antimicrobial therapy, reintubation, tracheostomy, prolonged hospital and ICU length of stay, and increased short- and long-term mortality.

Brodsky et al. [6] followed acute respiratory distress syndrome (ARDS) survivors (n=37) with symptoms of dysphagia after oral intubation prospectively over a 5-year period post discharge. They found that the median time to recovery was three months (IQR 3-6) with 23% of survivors having symptoms persisting more than six months. All resolved within 5 years after hospital discharge.

Prone positioning has been found to reduce mortality among patients with moderate-to-severe ARDS [7] and has become standard of care for Covid-19 patients. There is presently no data on whether or not prone positioning affects swallowing function post mechanical ventilation in general, nor if COVID-19 patients are particularly vulnerable due to their frequent need for prolonged ICU-stays.

Dysphagia assessment and treatment are in general done by a specialist, often a speech and language pathologist (SLP), but it can also be performed by other professions (e.g., phoniatricians, otolaryngologists, occupational therapists or critical care physicians) [4]. An instrumental evaluation is often recommended as a complement to a clinical bedside examination [8] with either a flexible endoscopic evaluation of swallowing (FEES) or with videofluoroscopy (also called Modified Barium Swallow, MBS). However, both methods are considered aerosol generating procedures (AGP) and these were restricted during the COVID-19 pandemic [9].

Dysphagia has been identified as one of the most important sequelae of severe and critical forms of COVID-19 [10], however the magnitude of short and long term dysphagia in COVID-19 are not yet known.

The aims of this study were threefold: to determine the incidence and grade of dysphagia in patients with COVID-19 after mechanical ventilation using level of oral intake, to determine recovery rate, and to explore risk factors associated with dysphagia.

In this paper, the terms dysphagia and swallowing dysfunction will be used synonymously.

Materials and methods

Participants

This was a longitudinal cohort study of consecutive patients ≥18 years with positive real-time reverse-transcriptase polymerase chain reaction test (RT-qPCR test) for SARS-CoV-2 admitted to three ICUs in the region (285 452 inhabitants). Patients who contracted COVID-19 while already in the hospital were excluded. Patients were referred to the SLP departments post mechanical ventilation between March 5 and July 5 2020 (5 days/week

service) for an evaluation of swallowing function before commencing oral diet. This is a substudy of the *Gävleborg COVID-19 cohort study*. Data regarding age, clinical frailty evaluated with the Clinical Frailty Score (CFS) [11] smoking, respiratory and swallowing parameters, comorbidities, days with tracheostomy, total days with ventilator, total days of hospitalization, prone position and days between extubation/decannulation and bedside swallowing evaluation were recorded. Body mass index (BMI) was calculated from body weight in kilograms divided by height in meters squared (self-reported or from medical chart), kg/m^2.

Setting

Patients were evaluated by an SLP either at the ICU, or at the High Dependency Unit (HDU) or COVID-19 ward after being transferred from the ICU. Recommendations were subsequently given regarding oral intake of medication, liquids, and food. The patients were monitored until return of safe oral feeding or until discharged to a rehabilitation clinic.

Bedside Swallowing Evaluation (BSE)

A BSE was performed when the patients were deemed medically stable and awake post mechanical ventilation. It was performed with the patient in an upright position. Assessed domains included an examination of motor (strength, speed, and range of movement) and sensory function of intra-oral musculature, cranial nerve examination, respiratory function, ability to follow single-step verbal commands, dentition, cough quality and dysphonia. Pulse oximetry was performed, and oxygen support and respiratory rate was recorded. The patients were observed swallowing different liquids, consistencies and volumes ad modum the Volume Viscosity Swallowing Test (V-VST)[12] but adding a solid bolus (typically a dry cracker) and adding a larger volume of water (100 ml) when appropriate [13]. Clinical signs

of impaired safety of swallowing (cough, decrease in oxygen saturation or change in voice quality) and impaired efficacy (bolus retention, posterior bolus leak, multiple re-swallows, and difficulty initiating a swallow) were analysed and when possible laryngeal palpation. Oral intake recommendations were based on a patient's swallowing ability in combination with other factors such as delirium, postural control, and fatigue.

The Functional Oral Intake Scale, FOIS

The Functional Oral Intake Scale, (FOIS) [14], is the most frequently used scale for evaluation of oral intake and was used as an outcome measure of swallow function. FOIS is a validated 7-point ordinal scale ranging from level 1 (nothing by mouth), level 2-3 (tube dependent), level 4 (total oral intake of a single consistency), level 5 (total oral intake of multiple consistencies requiring special preparation), level 6 (total oral intake with no special preparations, but minimal restrictions) to a score of 7 (total oral diet with no restrictions). Patients were stratified according to swallowing function where FOIS level 1-5 was defined as having dysphagia and level 6-7 as having a functional swallowing. The oral intake recommendation at hospital discharge was used to determine the secondary outcome measure.

Follow-up

All patients were invited to answer the 4-point swallowing questionnaire test (4QT) [15] 1-2 months post discharge from hospital or rehabilitation clinic.

Ethical considerations

The study was approved by the Swedish Ethical Authority (Dnr 2020-01746). Informed consent was obtained from all patients.

Statistical analysis

Normally distributed continuous data was presented as mean ± standard deviation and non-normally distributed data as median with IQR. Categorical data was presented as frequencies and percentage. The difference between groups was analysed with student t-test for normally distributed continuous data, with Mann Whitney *U*- test for non-normally distributed continuous data and Chi-2-test for categorical variables. The association between FOIS at ICU discharge (baseline) and number of days in hospital, number of days in the ICU, age, BMI, number of days intubated, prone position, frailty and tracheostomy were analysed using Spearman's rank correlation coefficient. A *p*-value of < 0.05 was regarded as significant. Statistical analyses were conducted using the software package Stata, version 16.1 (StataCorp LP; College Station, TX77845 USA).

Results

In total, 28 patients were included in the study (79% male, age 61 ±12 years; range 25-78, BMI 30 ±8 kg/m^2). Baseline characteristics are presented in Table 1. All patients lived at home and had a median clinical frailty score of 3 (range 1-5) before hospitalization with COVID-19. No patients had previous dysphagia or neurological diseases. Prone position was applied in 16 of 28 patients (57%), however length of time prone could not be determined from the medical records. Median length of ICU stay was 20 days (IQR 17-31) and median hospital stay was 35 days (IQR 27-52). Delirium was evident in 61% of the patients at BSE. During hospitalization, one patient died. Out of the surviving 27 patients, 41% (n=11) were discharged home and the remaining to specialized rehabilitation clinics.

Prevalence of dysphagia

Clinical signs of swallowing dysfunction (FOIS 1-5) were found in 20 of 28 patients (71%) (Table 1), median FOIS was 2 (IQR 1). Feeding tube dependency, complete or partial (FOIS 1-3) was seen in 57% of the patients (n=15). Three patients were assessed as FOIS 6 which means that some food or liquid items must be avoided. We chose to categorize them to the "functional swallowing group" since they were eating food from the regular hospital menu, only the easy to chew options.

The main presenting dysphagia symptoms were oral and pharyngeal muscle weakness (71%), cough (50%) and bolus retention (32%) (Table 2).

Patients with dysphagia were older (64 ±8.5 vs 53 ±16 years; p= 0.019), had a higher incidence of hypertension (70% vs 12%; p=0.006), remained with invasive ventilation (16 ±7 vs 10 ±2 days; p=0.017) or with tracheostomy (9.4 ±9.1 vs 1.1 ±2.2 days; p=0.03) longer. Median length of ICU stay (28.5, IQR 18.5 vs 15.5, IQR 4.5; p=0.001) and length of hospitalization (46.5, IQR 24.3 vs 24.0, IQR 10.3; p=0.003) were longer.

Respiratory function post mechanical ventilation

Fifty percent of the patients (n=14) had been tracheotomised (Table 1), but 11 of them were decannulated at the time of bedside evaluation. Reintubation occurred in seven (25%) of the patients and three times in one patient. Mean number of days from tracheostomy insertion to decannulation was 7 (SD 8.6). See Table 2 for respiratory vitals at BSE.

Recovery Rate

At discharge from hospital, all patients had been decannulated and 47% (n=9) of the patients with a FOIS of 1-5 at BSE had recovered a functional oral intake (FOIS 7). Of the 11 patients discharged home, one remained with restrictions in oral intake (FOIS 5). In the group going

to the rehabilitation clinic, 56% (nine of 16) remained with diet restrictions (FOIS 1-5) with four patients (15%) having complete or partial tube dependency (FOIS 1-3). Figure 1 shows the distribution of FOIS score at BSE and hospital discharge.

Follow-up

In total 79% (n=22) attended a follow-up visit 8 weeks (IQR 3.75) post discharge from the hospital. Of the six patients lost to follow-up one patient cancelled the appointment. The remaining five were lost due to death (n=1), patient returning to his home country (n=1), patient belonging to another region (n= 2) or patient being followed at the local clinic (n=1). Dysphagia had resolved in 13 of the 14 patients (93%) with the remaining patient reporting mild dysphagia symptoms. One of the patients in the "no dysphagia group" at discharge reported mild dysphagia symptoms at follow-up. The reported symptoms were: "it takes longer to eat meals than it used to" and "swallowing is effortful". Information on taste, smell, nutrition and voice complaints are reported in Table 3. If the patient had skipped a question and did not comment on it as being a problem in the conversation with the physician, it was scored as having no problem.

Associated risk factors

A moderate negative association was found between swallowing function at BSE and number of days in hospital (r=-0.471, p=0.01) Figure 2a, and number of days in the ICU (r=-0.48, p=0.01) Figure 2b, and also needing nutritional support at discharge (r=-0.445, p=0.02). There was a moderate association between FOIS at baseline and whether you were discharged home or to rehabilitation clinic (r-0.541, p=0.004). No significant associations were found between FOIS level at baseline and age, BMI, number of days intubated, prone position, CFS or having had a tracheostomy (p>0.05).

Discussion

This longitudinal cohort study found that dysphagia frequency post invasive mechanical ventilation in patients with COVID-19 was high, with an incidence of 71% requiring significant nutritional and swallowing interventions. This is in accordance with emerging data on this patient group [16]. Patients presented most frequently with signs of oral and pharyngeal muscle weakness at the BSE but also with significant fatigue and delirium, indicating that the dysphagia was multi-factorial.

Despite the average length of intubation far exceeding the time known to increase the risk of swallowing dysfunction [5] there was a rapid trajectory of improvement with the majority of patients (85%) having a full oral intake on one or multiple consistencies at discharge from hospital to the rehabilitation clinic (Figure 2). This is in accordance with results presented by Lima et al. [17] where 101 ICU patients diagnosed with COVID-19 were compared to 150 critical ICU patients with prolonged orotracheal intubation (≥ 48 hours) from the same institution. Dysphagia after prolonged intubation was common in both groups of their study. However, despite patients with COVID-19 remaining intubated longer than the other group they had less sustained dysphagia at discharge [17]. Dysphagia post mechanical ventilation can be multifactorial. It can be the direct result of the underlying problem requiring ICU admission (medical and/or surgical), but may also be acquired as a result of ICU care [18]. Further studies on the underlying causes of variations in dysphagia resolution are needed.

Frailty was screened on admission using the Clinical Frailty Scale (CFS) [11, 19], validated as a predictor of outcomes in older people. The CFS is now increasingly being used as a triage tool to make clinical decisions in the management of COVID-19 patients [19]. A CFS score of 5 is the most widely used cut off point to define frailty (1-3= fit, 4-5= pre-frail and ≥6 frail). In

this cohort 25/28 patients were categorized as fit and this might partly explain the rapid improvement and that no association was found between swallowing dysfunction and age or number of days invasively ventilated.

In total, 15 patients (57.1%) were completely or in part feeding tube dependent (FOIS 1-3) at the BSE but at hospital discharge this number had decreased to 4 patients (15%) and the rest (n=11) were discharged on an oral diet without feeding tube dependency either home or to specialized rehab. This demonstrates a rapid and progressive improvement in the cohort but does not provide detailed information regarding swallowing physiology since no instrumental evaluations were performed.

Emerging data suggests that prone positioning might not have the negative effect on swallowing that has been hypothesized [20]. If and how it influenced on swallowing function on this cohort cannot be established due to missing data in the medical charts.

Tracheostomy was performed in 50% of the patients. There was a good success of weaning, with the majority decannulated before the BSE and all patients decannulated at discharge. This is in accordance with the case series presented by Cardasis et al [21] where 74% of their 24 patients were decannulated at discharge from hospital. Like theirs, our cohort had a high baseline level of health with a median Clinical Frailty Score of 3 pre COVID-19.

Although dysphagia was common at bedside evaluation, the prognosis for resolution of dysphagic concerns seems good and recovery of swallowing function in COVID-19 patients after invasive mechanical ventilation was high. Only two patients reported some element of dysphagia at follow up. Contrastingly, 54% (n=12) reported dysphonia and were referred for SLP evaluation. This is consistent with emerging data from other countries [17, 20].

The factors most strongly associated with dysphagia in this cohort: prolonged hospital length of stay and ICU length of stay, did not differ from the review by Skoretz, Flowers and Martino or Brodsky et al. [5, 18] However, restrictions in oral intake seemed to resolve faster in this group of COVID-19 patients.

Strengths and weaknesses

The strengths of this study were the longitudinal design and that patient-related outcome measures (the 4QT) were collected at follow-up, which is valuable when determining patients' perception of their outcome. The study also had several limitations: it is a small sample size and only patients referred to SLP were included. Swallowing function was only measured by FOIS and although it is a validated way of estimating the functional eating ability of a patient, it does not analyse the biomechanical aspects of swallowing which is important when designing interventions for improving swallowing function. Nor does it take patients' subjective perception of swallowing in to consideration. However, oral intake is probably a more patient-centered and meaningful outcome compared to physiological swallow measures from the patient perspective, as argued by Regan et al [22]. When using a clinical judgement in (any) assessment of an impairment, there is always a risk of bias. In this study we used validated scales such as FOIS and the clinical frailty scale in an effort to control for inter-rater bias. Finally, follow-up data were based on patient-reported outcome measures, not a clinician rated scale, which means that there were some inconsistencies in how swallowing symptoms were expressed.

Conclusion:

In this study, the majority of COVID-19 patients needed precautionary measures to ascertain a safe oral intake post mechanical ventilation. We therefore recommend that screening of

swallowing function is added to the local ICU policies. In circumstances such as these, where the aerosol generating aspects are uncertain, best practice for assessing swallowing function in COVID-19 patients is a carefully executed BSE, to avoid further potential stressors on a reduced lung function.

Significance

The results provide new knowledge regarding prevalence, assessment and outcome for this new patient group, both to medicine in general and to speech pathology in Sweden. We have also gained new knowledge about factors associated with swallowing dysfunction.

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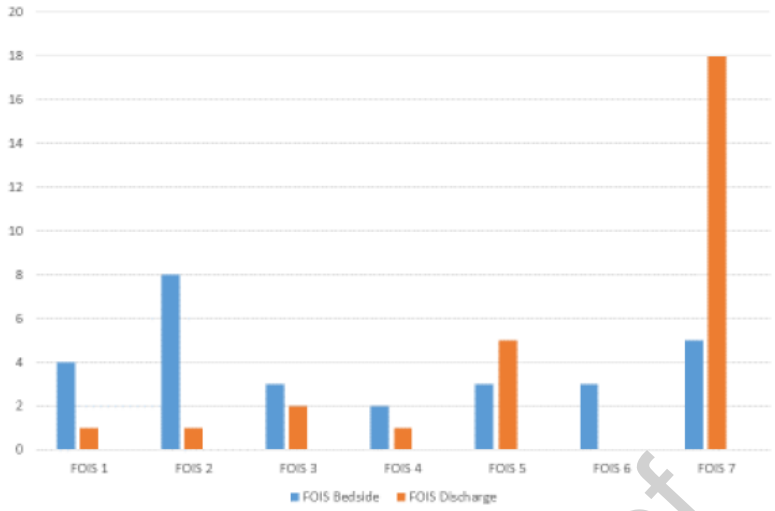
Figure legends

Figure 1. Number of patients with each Functional Oral Intake Scale (FOIS) score at Bedside Swallowing Evaluation and at hospital discharge.

Figure 2. Scatterplot with regression line depicting the relationship between Functional Oral Intake Scale (FOIS) level and: a) number of days in hospital and b) number of days in the Intensive Care Unit (ICU).



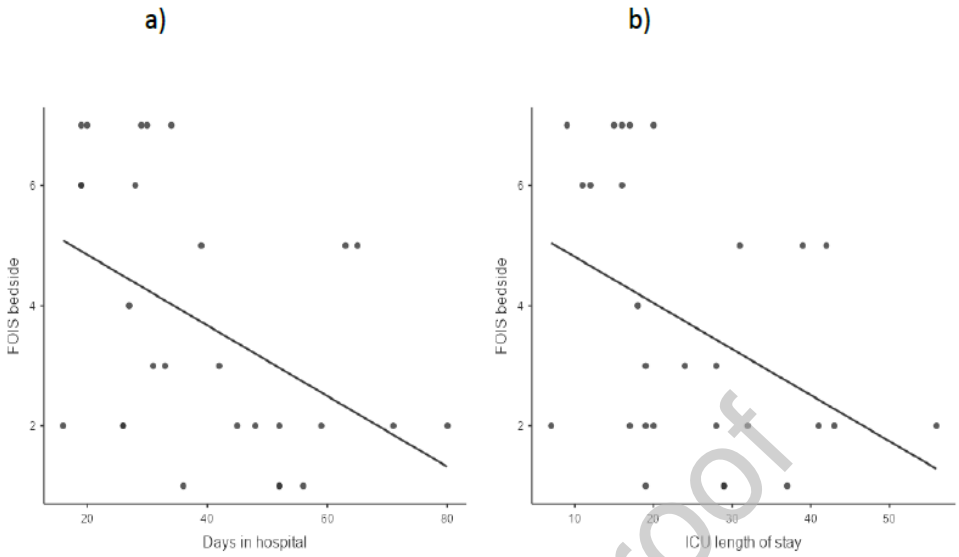


Table 1. Demographic and clinical characteristics stratified according to swallowing function at the Bedside Swallowing Evaluation.

Characteristics	Total	Functional swallow FOIS 6-7	Dysphagia, FOIS 1-5	p-value
	N=28	N=8	N=20	
Age, years, mean (SD)	61.0 (11.9)	52.9 (15.6)	64.2 (8.5)	**0.019**
Sex, male. % (n)	79% (22)	88% (7)	75% (15)	0.47
BMI (kg/m^2), mean (SD)	30.1 (7.9)	30.7 (10.8)	29.9 (6.7)	0.79
CFS, range 1-5. % (n)				0.44
1	4% (1)	12% (1)	0% (0)	
2	21% (6)	25% (2)	20% (4)	
3	64% (18)	50% (4)	70% (14)	
4	7% (2)	12% (1)	5% (1)	
5	4% (1)	0% (0)	5% (1)	
Smoking, % (n)				
Ex-smoker	35% (9)	38% (3)	33% (6)	
Never smoker	58% (15)	62% (5)	56% (10)	
Smoker	8% (2)	0% (0)	11% (2)	
Prone position, % (n)	57% (16)	38% (3)	65% (13)	0.18
Chronic cardiac disease, % (n)	14% (4)	0% (0)	20% (4)	0.17
Hypertension, % (n)	54% (15)	12% (1)	70% (14)	**0.006**
Diabetes, % (n)	21% (6)	12% (1)	25% (5)	0.47
Duration of orotracheal intubation, mean (SD)	14.1 (6.5)	9.6 (2.1)	15.9 (6.8)	**0.017**
Number of days in ICU, median (IQR)	20.0 (14.5)	15.5 (4.5)	28.5 (18.5)	**<0.001**
Tracheostomy, % (n)	50% (14)	25% (2)	60% (12)	0.094
Days with tracheostomy, mean (SD)	7 (8.6)	1.1 (2.2)	9.4 (9.1)	**0.03**
Number of days in hospital, median (IQR)	35.0 (25.3)	24.0 (10.3)	46.5 (24.3)	**0.003**
Number of days from extubation/decannulation to SLP evaluation, mean (SD)	3.4 (2.6)	4.6 (3.1)	3.0 (2.3)	0.12
Discharged home, % (n)	41% (11)	100% (8)	16% (3)	**<0.001**
Discharged to rehab, % (n)	59% (16)	0% (0)	84% (16)	**<0.001**
Diseased, % (n)	5% (1)	0% (0)	8% (1)	0.42

Data are presented as mean (standard deviation, SD), percentage (number) or median (Inter Quartile Range, IQR). FOIS= Functional Oral Intake Scale. CFS= Clinical Frailty Scale. SLP= Speech Language Pathologist. Significant p-values are reported in bold.

Table 2. Respiratory vitals and swallowing symptoms at SLP evaluation

Parameters	Total	Functional swallowing FOIS 6-7	Swallowing dysfunction FOIS 1-5	p-value
	N=28	N=8	N=20	
Respiratory vitals				
Breaths per minute	22.6 (4.0)	20.4 (2.2)	23.6 (4.2)	0.053
Oxygen saturation % (SD)	91.8 (17.8)	95.4 (2.2)	90.2 (21.4)	0.50
Oxygen by nasal cannula (n)	64% (18)	11% (3)	54% (15)	0.64
High Flow Nasal Cannula (n)	18% (5)	12% (1)	20% (4)	0.64
Swallowing and voice symptoms				
Posterior leak	25% (7)	12% (1)	30% (6)	0.26
Bolus retention	32% (9)	38% (3)	30% (6)	0.28
Multiple reswallows	21% (6)	38% (3)	15% (3)	0.26
Oral muscle weakness	71% (20)	25% (2)	90% (18)	<0.001
Weak mastication	29% (8)	38% (3)	25% (5)	<0.001
Cough	50% (14)	12% (1)	65% (13)	0.035
Wet voice	14% (4)	0% (0)	20% (4)	0.17
Drop in O2 saturation	7% (2)	12% (1)	5% (1)	0.15
Pharyngeal muscle weakness	71% (20)	25% (2)	90% (18)	<0.001
Fatigue	93% (26)	75% (6)	100% (20)	0.020
Dysphonia bedside	96% (27)	100% (8)	95% (19)	0.52

Data are presented as mean (standard deviation, SD) or percentage (number). FOIS= Functional Oral Intake Scale. SLP= Speech Language Pathologist.

Table 3. Patient-reported symptoms at follow up visit

n=22	None	Mild	Moderate
Dysgeusia (taste) % (n)	59% (13)	41% (9)	
Anosmia (Smell) % (n)	64% (14)	36% (8)	
*Nutritional problems % (n)	96% (21)	4% (1)	
Dysphonia % (n)	45% (10)	45% (10)	9% (2)

*Difficulty eating and drinking enough, weight loss.